EFFECT OF 2-METHOXY PHENACYL NICOTINIUM BROMIDE ON SERUM TOTAL CHOLESTEROL AND SERUM TRANSAMINASES

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SUMMARY: A derivative of nicotinic acid 2-methoxy Phenacyl Nicotinium Bromide was synthesized in our laboratory with the object to screen out its biochemical Pharmacological activities. The result of this compound was found to be highly significant as antilipemic, anticholesterolemic agent, but no significant effect was observed on Serum Glutamic Pyruvic Transaminase (SGPT) and Serum Glutamic Oxaloacetic Transaminase (SGOT).

Key Words: Anticholesterolemic agent, 2-methoxy phenacyl nicotinium bromide, serum transaminases.

INTRODUCTION

It has already been mentioned in the literature that nicotinic acid is a good cholesterol lowering agent (1) but with certain side effects (2). This research work was carried out with one of the object to prepare such an agent of nicotinic acid which could have a direct lowering effect on serum total cholesterol and no side effects. In this connection we have prepared a series of such compounds and in this paper we are reporting the activity of only one compound (i.e.) 2-methoxy Phenacyl Nicotinium Bromide on total serum cholesterol, serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) while its antilipemic activity has already published been (3).

The structure of newly synthesized compound was elucidated with the help of UV, IR, NMR and mass spectroscopy.

MATERIAL AND METHODS

The experiments were carried out on male rabbits with approximate weight 1.50 kg to 2.00 kg. The animals were grouped randomly, each comprised of five rabbits.

The group details and their treatment with the drug has already been described (3).

BIOCHEMICAL ANALYSIS

Five milliliter of blood from rabbits (non-fasting) was collected from the marginal ear vein on every 20th day up to 120 days (0, 20, 40, 60, 80, 100, 120) and then on every 10th day (130, 140, 150). The blood samples were centrifuged and serum was separated.

In these serum samples total cholesterol, SGPT and SGOT was determined according to the instruction sheets provided with reagent kits.

The values are expressed as the mean and standard error t-test is performed and p values were observed according to Bailey (4).

The reagent Kits and control Sera were supplied by Boehringer Mannheim (W. Germany). For the determination of total cholesterol, SGPT and SGOT reagent Kit having Cat. No. 237574, 487341 and 48733 respectively were used.

RESULT AND DISCUSSION

In view of the facts that extremely high concentration of total cholesterol in the blood is an independent risk factor for cardiac aliments and the cell surface receptor for a protein which carries cholesterol in blood are some how

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Table 1: Showing the effect of normal diet on the concentration of serum total cholesterol mg/100 ml in group 1 normal control (N.C) rabbits.

DAYS	1A	1B	1C	1D	1E	MEAN	SE
00	25.00	27.00	21.00	34.00	35.00	28.40	8.9
20	33.00	38.00	35.00	32.00	40.00	35.60	1.34
40	38.00	45.00	49.00	39.00	37.00	41.60	2.07
60	42.00	47.00	50.00	45.00	42.00	45.20	1.36
80	50.00	53.00	76.00	60.00	57.00	59.20	4.05
100	47.00	60.00	63.00	55.00	68.00	58.60	3.20
120	59.00	65.00	90.00	65.00	80.00	71.80	5.10
130	62.00	72.00	95.00	65.00	83.00	75.40	5.40
140	61.00	57.00	98.00	53.00	87.00	71.20	7.20
150	69.00	86.00	105.00	61.00	93.00	82.80	9.74

Table 2: Showing the effect of cholesterol/butter rich diet on the serum total cholesterol mg/100 ml in group 2 pathological control (P.C) rabbits.

DAYS	2A	2B	2C	2D	2E	MEAN	SE
00	19.00	28.00	34.00	24.00	30.00	27.00	2.29
20	63.00	75.00	97.00	90.00	80.00	81.00	5.78
40	110.00	220.00	171.00	110.00	225.00	167.20	19.20
60	155.00	380.00	243.00	365.00	310.00	290.60	37.17
80	236.00	507.00	357.00	487.00	368.00	391.00	43.99
100	398.00	683.00	482.00	590.00	425.00	515.60	47.63
120	551.00	612.00	655.00	800.00	615.00	646.60	46.60

Table 2A: Showing the effect of normal diet.

130	391.00	684.00	459.00	563.00	403.00	500.00	49.30
140	288.00	567.00	326.00	495.00	387.00	412.60	46.60
150	219.00	355.00	308.00	341.00	212.00	287.00	27.00

Table 3: Showing the effect of cholesterol/butter rich diet on the serum total cholesterol mg/100 ml in group 3 treated (T_1) rabbits.

DAYS	3A	3B	3C	3D	3E	MEAN	SE	p
00	31.00	29.00	34.00	29.00	25.00	29.60	1.31	
20	60.00	72.00	53.00	60.00	57.00	60.40	3.21	
40	172.00	184.00	201.00	197.00	201.00	191.00	5.50	
60	281.00	317.00	411.00	324.00	391.00	344.80	21.71	
80	315.00	414.00	533.00	387.00	442.00	418.20	32.27	
100	506.00	497.00	611.00	409.00	724.00	549.40	53.97	
120	600.00	317.00	702.00	508.00	946.00	614.60	78.00	

Table 3A: Effect of 2-methoxy Phenacyl Nicotinium Bromide 30 mg/day.

130	376.00	317.00	554.00	395.00	639.00	456.20	53.86	N.S
140	124.00	178.00	283.00	267.00	382.00	246.80	39.90	<.02
150	94.00	105.00	192.00	180.00	259.00	166.00	30.63	<.001

Table 4: Showing the effect of normal diet on SGPT mg/100 ml in group 1 normal control (N.C) rabbits.

DAYS	4A	4B	4C	4D	4E	MEAN	SE
00	58.00	58.00	80.00	63.00	42.00	60.20	6.08
20	64.00	76.00	88.00	67.00	49.00	68.80	6.47
40	66.00	81.00	82.00	69.00	55.00	70.60	5.02
60	75.00	90.00	76.00	75.00	58.00	74.80	5.07
80	76.00	97.00	80.00	72.00	67.00	78.40	5.12
100	80.00	95.00	87.00	70.00	73.00	81.00	4.57
120	82.00	85.00	92.00	74.00	75.00	81.60	3.32
130	78.00	86.00	94.00	80.00	77.00	83.00	3.16
140	80.00	88.00	100.00	88.00	73.00	85.80	4.52
150	89.00	85.00	97.00	91.00	75.00	87.40	3.65

Table 5: Showing the effect of cholesterol/butter rich diet on SGPT mg/100 ml in group 2 pathological control (P.C) rabbits.

DAYS	5A	5B	5C	5D	5E	MEAN	SE
00	82.00	55.00	58.00	67.00	78.00	68.00	5.31
20	84.00	57.00	64.00	68.00	77.00	70.00	4.76
40	88.00	58.00	66.00	75.00	81.00	73.60	5.31
60	91.00	61.00	75.00	78.00	85.00	78.00	5.07
80	93.00	66.00	76.00	76.00	88.00	79.80	4.80
100	96.00	78.00	80.00	82.00	88.00	84.80	3.26
120	101.00	83.00	82.00	89.00	93.00	89.60	3.48

Table 5A: Showing the effect of normal diet.

130	101.00	85.00	78.00	91.00	91.00	89.20	3.80
140	112.00	82.00	80.00	95.00	99.00	93.60	5.87
150	110.00	81.00	81.00	97.00	101.00	94.00	5.70

Table 6: Showing the effect of cholesterol/butter rich diet on SGPT mg/100 ml in group 3 treated (T_1) rabbits.

DAYS	6A	6B	6C	6D	6E	MEAN	SE	p
00	59.00	68.00	81.00	73.00	41.00	64.40	6.85	
20	57.00	75.00	79.00	80.00	44.00	67.00	7.03	
40	56.00	88.00	79.00	85.00	52.00	72.00	7.51	
60	68.00	85.00	78.00	91.00	50.00	75.20	6.18	
80	69.00	89.00	80.00	97.00	66.00	80.20	5.86	
100	72.00	87.00	77.00	97.00	69.00	80.40	5.15	
120	78.00	92.00	76.00	99.00	73.00	83.60	5.04	

Table 6A: Effect of 2-methoxy Phenacyl Nicotinium Bromide 30 mg/day.

130	83.00	91.00	80.00	96.00	75.00	85.00	3.78	N.S
140	82.00	93.00	85.00	98.00	72.00	86.00	4.50	N.S
150	87.00	98.00	83.00	91.00	72.00	86.20	4.32	N.S

Table 7: Showing the effect of normal diet on SGOT mg/100 ml in group 1 normal control (N.C) rabbits.

DAYS	7A	7B	7C	7D	7E	MEAN	SE
00	39.00	48.00	66.00	52.00	37.00	48.40	4.65
20	39.00	59.00	64.00	58.00	41.00	52.20	4.55
40	45.00	47.00	45.00	51.00	50.00	47.60	1.11
60	40.00	45.00	56.00	53.00	44.00	47.60	2.66
80	37.00	51.00	62.00	60.00	57.00	53.40	4.02
100	35.00	50.00	67.00	62.00	45.00	51.80	5.16
120	38.00	43.00	64.00	69.00	44.00	51.60	5.56
130	40.00	38.00	67.00	61.00	48.00	50.80	5.11
140	42.00	38.00	70.00	64.00	48.00	52.40	5.58
150	45.00	36.00	71.00	67.00	45.00	52.80	6.12

Table 8: Showing the effect of cholesterol/butter rich diet on SGOT mg/100 ml in group 2 pathological control (P.C) rabbits.

DAYS	8A	8B	8C	8D	8E	MEAN	SE
00	32.00	57.00	43.00	24.00	26.00	36.40	5.47
20	35.00	55.00	43.00	33.00	24.00	38.00	4.66
40	34.00	55.00	44.00	30.00	29.00	38.40	4.40
60	54.00	60.00	42.00	37.00	31.00	44.80	4.79
80	54.00	65.00	44.00	44.00	40.00	49.40	4.05
100	58.00	69.00	47.00	45.00	45.00	52.80	4.21
120	64.00	76.00	55.00	53.00	59.00	61.40	3.67

Table 8A: Showing the effect of normal diet.

130	65.00	72.00	57.00	51.00	60.00	61.00	3.18
140	67.00	75.00	58.00	55.00	57.00	62.40	3.36
150	64.00	75.00	60.00	56.00	64.00	63.80	2.83

Table 9: Showing the effect of cholesterol/butter rich diet on SGOT mg/100 ml in group 3 treated (T_1) rabbits.

DAYS	9A	9B	9C	9D	9E	MEAN	SE	p
00	64.00	38.00	27.00	31.00	29.00	37.80	6.08	
20	67.00	45.00	36.00	39.00	27.00	42.80	9.08	
40	71.00	51.00	40.00	46.00	33.00	48.20	5.76	
60	75.00	63.00	50.00	51.00	37.00	55.20	5.75	
80	79.00	75.00	57.00	59.00	44.00	62.80	5.70	
100	81.00	74.00	55.00	63.00	45.00	63.60	5.76	
120	82.00	71.00	59.00	65.00	43.00	64.00	5.72	

Table 9A: Effect of 2-methoxy Phenacyl Nicotinium Bromide 30 mg/day.

130	79.00	75.00	63.00	60.00	45.00	64.40	5.37	N.S
140	80.00	76.00	65.00	57.00	47.00	65.00	5.41	N.S
150	80.00	77.00	69.00	53.00	49.00	65.60	5.59	N.S

necessary for the egulation of blood cholesterol level, the derivitization of Nicotinic acid a well known lipid lowering agent was done which could possibly regulate the synthesis, transport and deposition of cholesterol.

There are various mechanisms attributed to the lipid lowering effect of nicotinic acid, according to Altschull (5) hypocholesterolemic activity of Nicotinic acid might be related to the increased oxidation of cholesterol.

While another mechanism of lipolytic effect has been suggested to be dependent upon the reduction of the increased cyclic AMP level induced by lipolytic hormones, Butcher (6) demonstrated that is the cyclic AMP level in adipocytes was elevated by a combined action of Noradrenaline and caffeine, this increase in cAMP was reduced by nicotinic acid. Almost all investigators agreed that in the majority of hypercholesterolemic subject blood cholesterol level can be moderately reduced by the treatment of nicotinic acid in one or other way.

The result of newly synthesized compound is also very significant in respect to its hypocholesterolemic activity. The compound (i.e) 2-methoxy Phenacyl Nicotinium Bromide reduced the amount of total cholesterol in T_1 group from 614 mg/100 ml to 166 kg/ml ($p<0.001$) as compared to pathological (P.C) values (i.e.) from 646 mg/100 ml to 287 mg/100 ml.

These results provide us statistical significance and the efficacy of the compound on lowering of serum cholesterol values.

There is no significant change was observed in the values of SGPT and SGOT in treated group (i.e.) T_1 in comparison to pathological control (i.e) P.C and normal control (i.e) N.C. through out the whole period of 150 days.

The values of SGPT are 83.60 to 86.20 mg/100 ml (T_1), 89.60 to 94.00 mg/100 ml (P.C), 81.60 to 87.40 mg/100 ml (N.C) respectively.

The values of SGOT are 64.00 to 65.60 mg/100 ml (T_1), 61.40 to 63.80 mg/100 ml (P.C) and 51.60 to 52.80 mg/100 ml (N.C) respectively. Our results are also supported by the work of Carlson and Anders (7,8).

The effect of various other derivatives of nicotinic acid synthesized in our laboratory on different parameters have already been published (9,10).

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